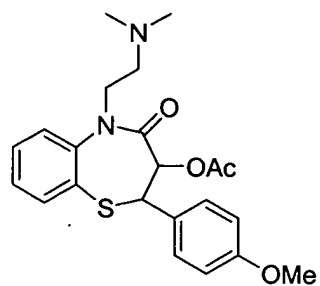
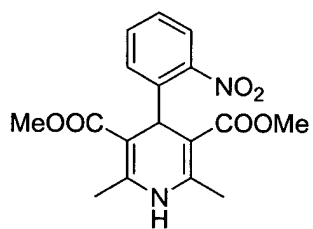


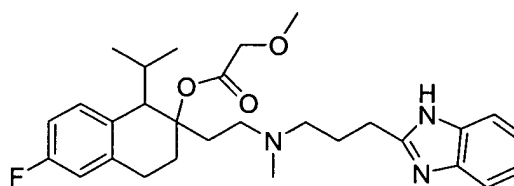
Verapamil



Diltiazem

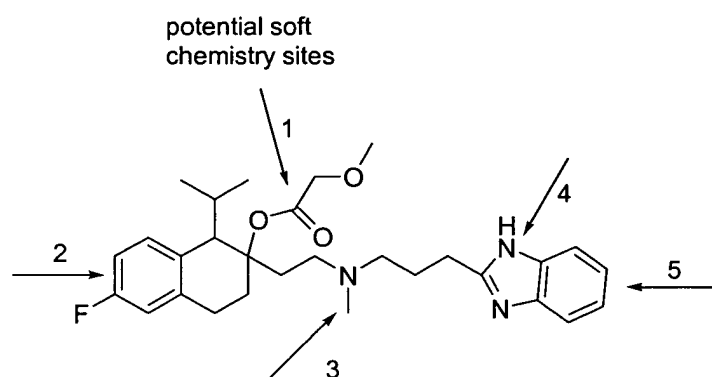


Nifedipine



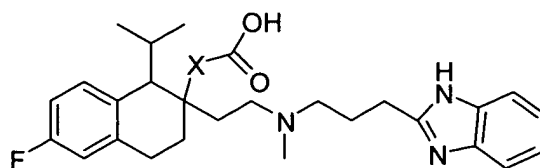
Mibefradil

Figure 1

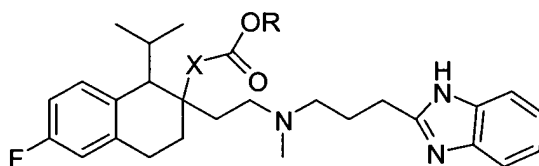
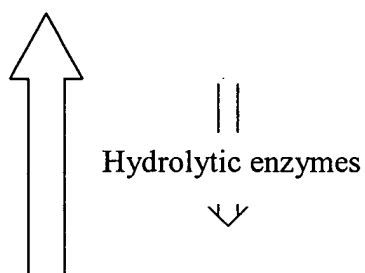


Mibefradil

Figure 2

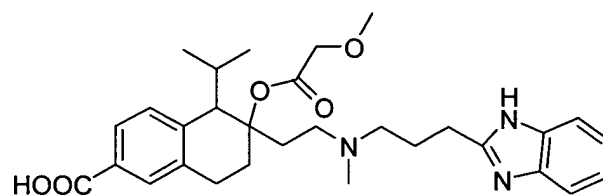


primary inactive metabolite
X = bond, CH₂, or OCH₂

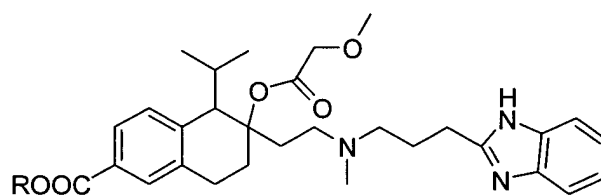
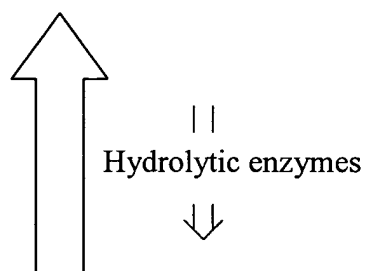


soft analog
R = lower alkyl optionally
substituted by OH or NH₂,
X is as defined above

Figure 3

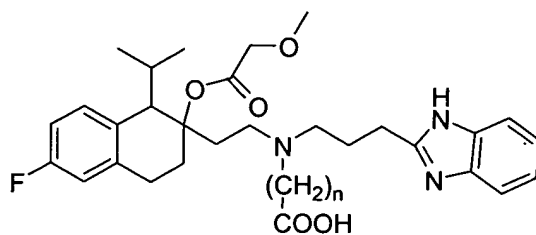


primary inactive metabolite

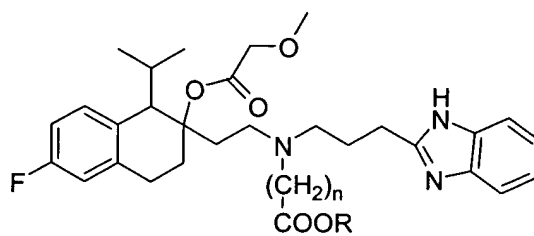
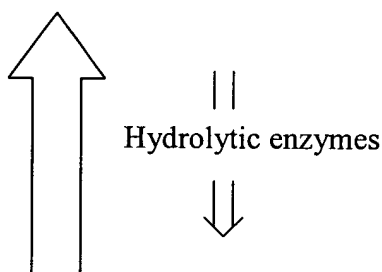


soft analog
R = lower alkyl optionally
substituted by OH or NH₂

Figure 4

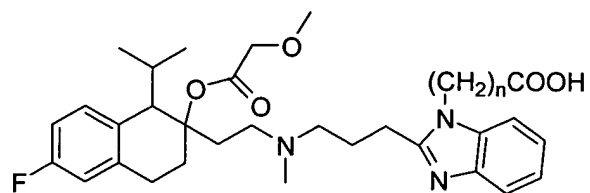


primary inactive metabolite
n = 1 to 3

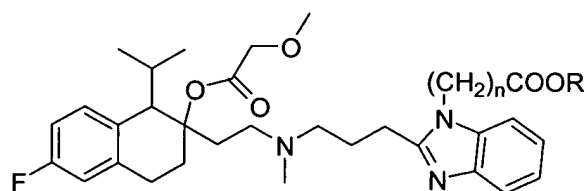
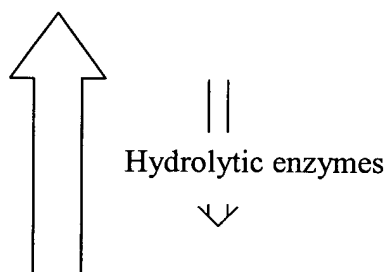


soft analog
n = 1 to 3
R = lower alkyl optionally
substituted by OH or NH₂

Figure 5

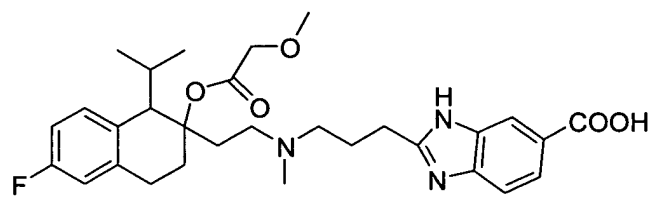


primary inactive metabolite
n = 1 to 3

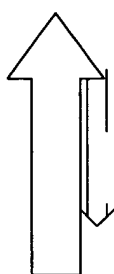


soft analog
n = 1 to 3
R = lower alkyl optionally
substituted by OH or NH₂

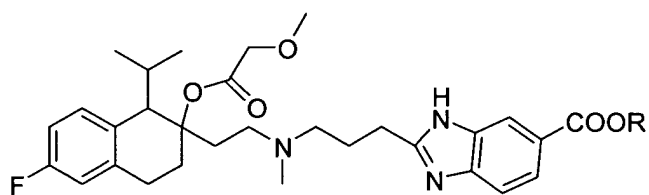
Figure 6



primary inactive metabolite

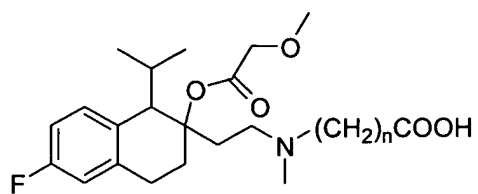


Hydrolytic enzymes

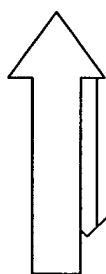


soft analog
R = lower alkyl optionally
substituted by OH or NH₂

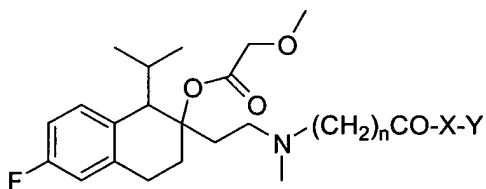
Figure 7



primary inactive metabolite
n = 1 to 3

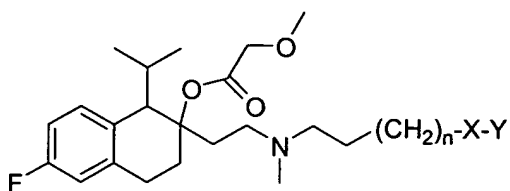


Hydrolytic enzymes



soft analog
n = 1 to 3
X = O, NH, NR where R
is lower alkyl
Y = optionally substituted aryl
or heterocyclyl

Figure 8



primary inactive metabolite

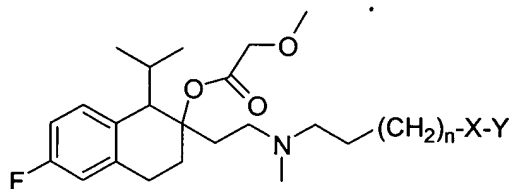
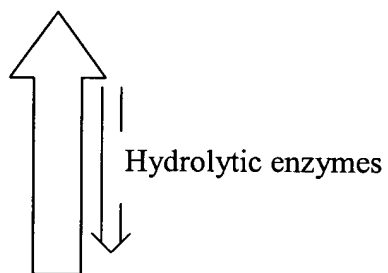
$n = 0$ to 2

$X = O, S, SO, SO_2, NH, NR$ or $N(CH_2)_mCOOH$

where m is 0 or 2

$Y =$ aryl or heterocyclyl substituted with $(CH_2)_mCOOH$

where m is 0 to 2



soft analog

$n = 0$ to 2

$X = O, S, SO, SO_2, NH, NR$ or $N(CH_2)_mCOOR$

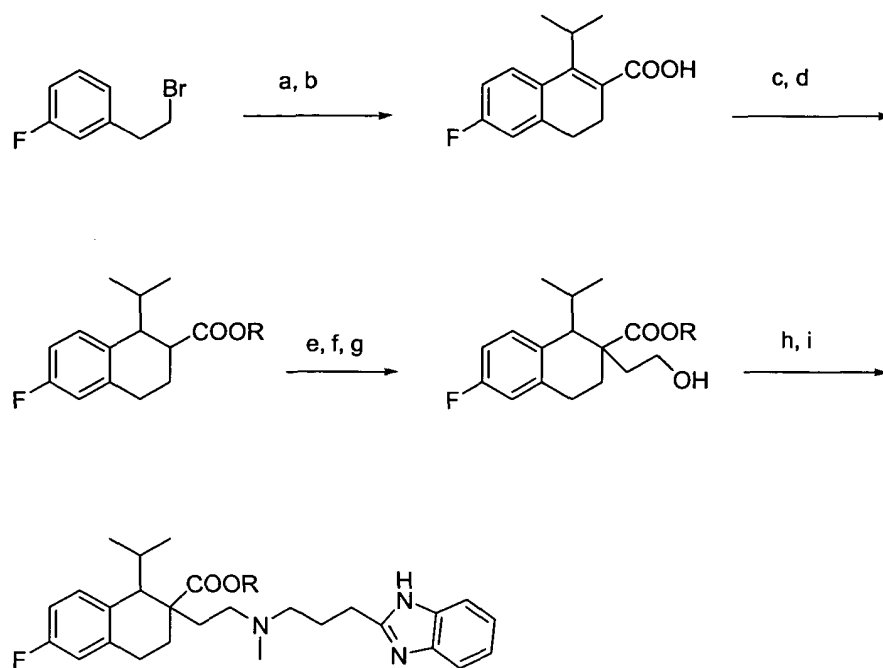
where m is 0 or 2

$Y =$ aryl or heterocyclyl substituted with $(CH_2)_mCOOR$

where m is 0 to 2

$R =$ lower alkyl optionally substituted by OH or NH_2

Figure 9



a, $i\text{PrCOCH}_2\text{COOEt}$, NaOEt ; b, $\text{conc. H}_2\text{SO}_4$; c, ROH , H^+ ; d, H_2 , Pd/C ; e, LDA ; f, $\text{BrCH}_2\text{CH}_2\text{OTHP}$; g, H^+ ; h, TsCl , TEA ; i, $2\text{-(N-methylaminopropyl)benzimidazole}$, K_2CO_3

Figure 10

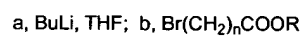
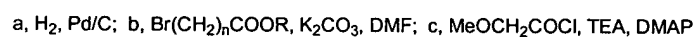


Figure 11

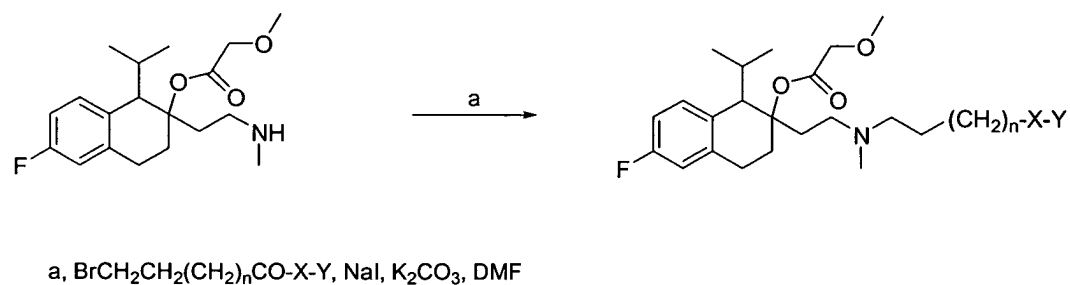
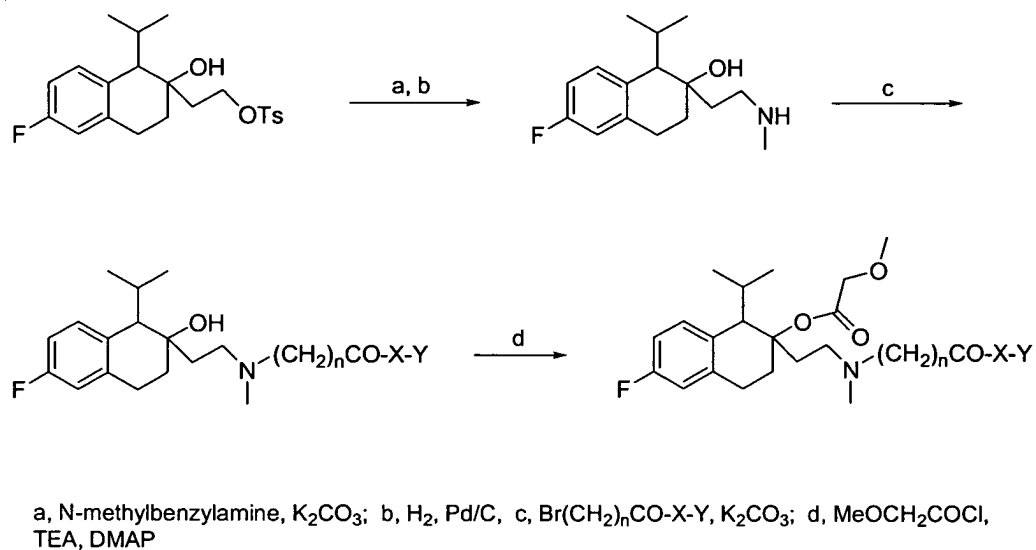


Figure 12